



NIAID CLINICAL RESEARCH STANDARDS

The NIAID Clinical Research Standards provide a framework to promote scientifically sound and ethically responsible research. The Standards are grouped into four key areas:

1. Clinical Research Development, Review, Conduct and Oversight;
2. Clinical Research Management;
3. Training and Education; and
4. Quality Assurance/Quality Control.

While this framework defines requirements for maximizing the quality of NIAID clinical research, it also provides flexibility to account for the diverse contexts in which NIAID research is conducted.

The scope of these standards includes all clinical research activities as defined in the NIH Grants and Funding Glossary definition of Clinical Research located at <https://grants.nih.gov/grants/glossary.htm>

Research with human subjects that is:

1. Patient-oriented research. Research conducted with human subjects (or on material of human origin such as tissues, specimens, and cognitive phenomena) for which an investigator (or colleague) directly interacts with human subjects. Excluded from this definition are in vitro studies that utilize human tissues that cannot be linked to a living individual. It includes:
 - mechanisms of human disease
 - therapeutic interventions
 - clinical trials
 - development of new technologies
2. Epidemiological and behavioral studies.
3. Outcomes research and health services research.

Studies falling under 45 CFR part 46.101(b) (4) (Exemption 4) are not considered clinical research by this definition.

1. CLINICAL RESEARCH DEVELOPMENT, REVIEW, CONDUCT AND OVERSIGHT

STANDARD 1.1

Each Division will have established protocol development and implementation tools [e.g., templates for protocols, informed consent, manual of operations, standard operating procedures (SOPs), guidelines, case report forms and safety reports].

PURPOSE: To assist investigators in developing and implementing quality clinical research protocols in accordance with applicable regulations and guidance.

RELATED NIH and NIAID DOCUMENTS:

- See Division websites for division-specific protocol templates
- FDA / NIH clinical trial protocol template for phase 2/3 studies (optional), located at: <http://osp.od.nih.gov/office-clinical-research-and-bioethics-policy/clinical-research-policy/clinical-trials>

STANDARD 1.2

Each Division will have policies, guidelines and/or standard operating procedures, for:

- **Scientific review (including biostatistical review)**
- **Regulatory review**
- **Institutional Review Board (IRB)/Ethics Committee (EC) review**
- **Conflict of Interest (COI) review**
- **Site Monitoring**
- **Safety/data monitoring review including trial-specific study progress and safety monitoring plans to be submitted by the study team for Division approval, and**
- **Study participant outreach activities to maximize recruitment, retention and community involvement**
- **Data Sharing**
- **Open access to study results**

PURPOSE: To ensure regulatory compliance and reduce risks to subjects: scientific review ensures scientific quality, the importance to clinical practice, and the appropriateness of the study to the sponsoring entity; IRB/EC review ensures study participant safety and good ethical conduct of the study; COI reviews help to minimize bias and ensure the public trust in government-sponsored research; Independent site monitoring is essential for all clinical trials involving investigational drugs, devices, or biologics and other clinical research, including research of licensed products, perceived to involve more than a minimal risk; Safety and data monitoring are essential to monitor study participant safety, ensure integrity of the research

study and evaluate the efficacy of the intervention; Research participants involvement in clinical research development promotes sound ethical science; Data sharing reinforces open scientific inquiry, encourages diversity of analysis and opinion, promotes new research, and increases public trust; Open access to study results of clinical research contributes to the general body of science and ultimately, to public health and safety.

RELATED NIH and NIAID POLICY DOCUMENTS:

- NIH Policy on the Use of a Single Institutional Review Board for Multi-Site Research, June 21, 2016, NOT-OD-16-094 (<https://grants.nih.gov/grants/guide/notice-files/NOT-OD-16-094.html>)
- NIH Policy on the Dissemination of NIH-Funded Clinical Trial Information, September 16, 2017, NOT-OD-16-149 (Describes requirements for ClinicalTrials.gov registration and results reporting) (<https://grants.nih.gov/grants/guide/notice-files/NOT-OD-16-149.html>)
- NIAID Policy on Data and Safety Monitoring Board (DSMB) Operations (<https://www.niaid.nih.gov/research/guidance-policies-and-standard-operating-procedures>)
- NIAID Policy for Identifying Potential Conflict of Interest for Individuals Serving on Advisory Committees or Independent Safety Monitors Responsible for Data and Safety Monitoring of Clinical Trials (<https://www.niaid.nih.gov/research/guidance-policies-and-standard-operating-procedures>)

2. CLINICAL RESEARCH MANAGEMENT

STANDARD 2.1

Each Division will have policies, guidelines and/or SOPs for site establishment, approval of study initiation and for initial and ongoing site evaluation including minimal standards for operations (e.g., site staffing, training, facilities, data management, pharmacy and laboratory management, specimen handling, record keeping and safety reporting).

PURPOSE: To ensure that sites are qualified and ready to conduct a particular NIAID funded clinical research study.

STANDARD 2.2

Each Division will have policies, guidelines/SOPs that describe their requirements for clinical data management system/infrastructure including policies, guidelines/SOPs for data collection, data integrity, and data security.

PURPOSE: To ensure that the results of research are carefully recorded in a form that will allow accuracy and access for analysis and review.

Web link for reference related to Computerized Systems (data management) for FDA regulated research studies: <http://www.fda.gov/OHRMS/DOCKETS/98fr/04d-0440-gdl0002.pdf>

STANDARD 2.3

Each Division will have policies, guidelines/SOPs that specify safety reporting procedures including Adverse Events (AEs), Serious Adverse Events (SAEs), Serious and Unexpected Suspected Adverse Reactions (SUSARs), Unanticipated Problems (UPs) and Unanticipated Adverse Device Effect (UADE) reporting. These reporting policies, guidelines/SOPs should be specific in definitions/ categorizations of events, use of specific required forms, timing of reports, and identification of specific accountability for submission, review and follow up action.

PURPOSE: To ensure that mechanisms and procedures are in place to protect the safety of participants in NIAID-supported clinical research.

Web Links for references related to safety reporting:

- FDA Guidance for Clinical Investigators, Sponsors, and IRBS: Adverse Event Reporting to IRBs – Improving Human Subject Protection (January 2009) (<http://www.fda.gov/downloads/RegulatoryInformation/Guidances/UCM126572.pdf>)
- HHS OHSRP Unanticipated Problems Involving Risks and Adverse Events Guidance (2007) (<https://www.hhs.gov/ohrp/regulations-and-policy/guidance/reviewing-unanticipated-problems/>)
- FDA Guidance for Industry and Investigators: Safety Reporting Requirements for INDs and BA/Be Studies (December 2012) (<https://www.fda.gov/downloads/Drugs/Guidances/UCM227351.pdf>)

3. *TRAINING AND EDUCATION*

STANDARD 3.1

Each Division will establish minimal standards for training Division staff and clinical site staff in good clinical practice (GCP), human subjects protection (HSP), relevant clinical laboratory practices and relevant Institute and Division policies.

PURPOSE: To communicate the expectations of acceptable practice in conducting clinical research and human subject protections.

RELATED NIH and NIAID POLICY DOCUMENTS AND LINKS:

- Policy on Good Clinical Practice Training for NIH Awardees Involved in NIH-funded

Clinical Trials (NOT-OD-16-148) (<https://grants.nih.gov/grants/guide/notice-files/NOT-OD-16-148.html>)

- NIAID GCP Training Policy (<https://www.niaid.nih.gov/research/guidance-policies-and-standard-operating-procedures>)
- NIAID GCP Training (<https://gcplearningcenter.niaid.nih.gov/Pages/default.aspx>)
- NIAID DSMB Training (<https://dsmblearningcenter.niaid.nih.gov/Pages/default.aspx>)

4. QUALITY ASSURANCE AND QUALITY CONTROL

STANDARD 4.1

Each Division will have policies, guidelines to ensure that quality assurance and quality control processes are established in their Division and clinical research sites.

PURPOSE: To ensure adherence to relevant clinical research-related laws, regulations and guidelines as well as NIH, NIAID, and Division policies and standards; and to identify and resolve problems at their early stages.